

What Is Claimed Is:

1. A combination comprising a first amount of  
5 an aldosterone receptor antagonist and a second amount  
of a beta-adrenergic antagonist, wherein said  
aldosterone receptor antagonist and beta-adrenergic  
antagonist together comprise a therapeutically-effective  
amount of said aldosterone receptor antagonist and said  
10 beta-adrenergic antagonist.

2. The combination of Claim 1 wherein said  
aldosterone receptor antagonist is selected from epoxy-  
containing compounds.  
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3. The combination of Claim 2 wherein said  
epoxy-containing compound has an epoxy moiety fused to  
the "C" ring of the steroidal nucleus of a 20-spiroxane  
compound.  
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4. The combination of Claim 3 wherein said  
20-spiroxane compound is characterized by the presence  
of a 9a-,11a-substituted epoxy moiety.

5. The combination of Claim 2 wherein said  
epoxy-containing compound is selected from the group  
consisting of:

pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-  
30 17-hydroxy-3-oxo,g-lactone, methyl ester, (7a,11a,17a)-;

pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-  
17-hydroxy-3-oxo-dimethyl ester, (7a,11a,17a)-;

35 3'H-cyclopropa[6,7] pregna-4,6-diene-21-carboxylic acid,  
9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-,g-  
lactone, (6b,7b,11b,17b)-;

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pregn-4-ene-7,21-dicarboxylic acid,9,11-  
epoxy-17-hydroxy-3-oxo-,7-(1-methylethyl) ester,  
monopotassium salt,(7a,11a,17a)-;

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pregn-4-ene-7,21-dicarboxylic acid,9,11,-epoxy-  
17-hydroxy-3-oxo-,7-methyl ester, monopotassium  
salt, (7a,11a,17a)-;

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3'H-cyclopropa[6,7]pregna-1,4,6-triene-21-  
carboxylic acid, 9,11-epoxy-6,7-dihydro-17-  
hydroxy-3-oxo-,g-lactone(6a,7a,11.a)-;

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3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic  
acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-,  
methyl ester, (6a,7a,11a,17a)-;

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3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic  
acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-,  
monopotassium salt, (6a,7a,11a,17a)-;

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3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic  
acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-,g-  
lactone, (6a,7a,11a.,17a)-;

pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-  
17-hydroxy-3-oxo-,g-lactone, ethyl ester,  
(7a,11a,17a)-; and

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pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-  
17-hydroxy-3-oxo-,g-lactone, 1-methylethyl  
ester,(7a,11a,17a)-.

6. The combination of Claim 4 wherein said  
35 epoxy-steroidal-type compound is eplerenone.

7. The combination of Claim 6 wherein said  
beta-adrenergic antagonist is selected from the group

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consisting of acebutolol, alprenolol, amosulalol, arotinolol, atenolol, befunolol, bevantolol, bisoprolol, bopindolol, bucumolol, bucindolol, bunitrolol, butofilolol, carteolol, carvedilol, celiprolol, 5 cloranolol, indenolol, labetalol, levoprolol, mepindolol, metipranolol, metoprolol, nadolol, nebivolol, nifenalol, oxprenolol, penbutolol, pindolol, propranolol, sotalol, timolol, toprol, and viskenit.

10 8. The combination of Claim 6 wherein said beta-adrenergic antagonist is selected from the group consisting of Acc 9369, AMO-140, betaxolol, capsinolol, carazolol, CP-331684, diprafenone, ersentilide, esmolol, esprolol, Fr-172516, ISV-208, L-653328, laniolol, 15 levobunolol, LM-2616, nipradilol, Pharmaprojects No 5279, S-atenolol, SB-226552, SR-58894A, SR-59230A. talinolol, tertatolol, tilisolol, TZC-5665, UK-1745, xamoterol, and YM-430.

20 9. The combination of Claim 7 further characterized by said beta-adrenergic antagonist and said epoxy-steroidal aldosterone receptor antagonist being present in said combination in a weight ratio range from about one-to-one to about one-to-twenty of 25 said beta-adrenergic antagonist to said aldosterone receptor antagonist.

10 10. The combination of Claim 9 wherein said weight ratio range is from about one-to-five to about 30 one-to-fifteen.

11. The combination of Claim 10 wherein said weight ratio range is about one-to-ten.

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12. The combination of Claim 6 wherein the beta-adrenergic antagonist comprises carvedilol or a pharmaceutically-acceptable salt thereof.

5 13. The combination of Claim 6 wherein the beta-adrenergic antagonist comprises metoprolol or a pharmaceutically-acceptable salt thereof.

10 14. The combination of Claim 6 wherein the beta-adrenergic antagonist comprises bisoprolol or a pharmaceutically-acceptable salt thereof.

15 15. The combination of Claim 6 wherein the beta-adrenergic antagonist comprises bucindolol or a pharmaceutically-acceptable salt thereof.

20 16. The combination of Claim 6 wherein the beta-adrenergic antagonist comprises propranolol or a pharmaceutically-acceptable salt thereof.

17. The combination of Claim 6 wherein the beta-adrenergic antagonist comprises esmolol or a pharmaceutically-acceptable salt thereof.

25 18. The combination of Claim 6 wherein the beta-adrenergic antagonist comprises acebutolol or a pharmaceutically-acceptable salt thereof.

30 19. The combination of Claim 6 wherein the beta-adrenergic antagonist comprises sotalol or a pharmaceutically-acceptable salt thereof.

35 20. The combination of Claim 6 wherein the beta-adrenergic antagonist comprises labetalol or a pharmaceutically-acceptable salt thereof.

21. The combination of Claim 1 wherein said aldosterone antagonist is spironolactone.

22. The combination of Claim 21 wherein  
5 said beta-adrenergic antagonist is selected from the group consisting of acebutolol, alprenolol, amosulalol, arotinolol, atenolol, befunolol, bevantolol, bisoprolol, bopindolol, bucumolol, bucindolol, bunitrolol, butofilolol, carteolol, carvedilol, celiprolol,  
10 cloranolol, indenolol, labetalol, levoprolol, mepindolol, metipranolol, metoprolol, nadolol, nebivolol, nifenalol, oxprenolol, penbutolol, pindolol, propranolol, sotalol, timolol, toprol, and viskenit.

23. The combination of Claim 21 wherein said  
15 beta-adrenergic antagonist is selected from the group consisting of Acc 9369, AMO-140, betaxolol, capsinolol, carazolol, CP-331684, diprafenone, ersentilide, esmolol, esprolol, Fr-172516, ISV-208, L-653328, laniolol,  
20 levobunolol, LM-2616, nipradilol, Pharmaprojects No 5279, S-atenolol, SB-226552, SR-58894A, SR-59230A. talinolol, tertatolol, tilisolol, TZC-5665, UK-1745, xamoterol, and YM-430.

24. The combination of Claim 22 further  
25 characterized by said beta-adrenergic antagonist and said aldosterone receptor antagonist being present in said combination in a weight ratio range from about one-to-one to about one-to-twenty of said beta-adrenergic  
30 antagonist to said aldosterone receptor antagonist.

25. The combination of Claim 24 wherein said weight ratio range is from about one-to-five to about one-to-fifteen.

26. The combination of Claim 25 wherein said weight ratio range is about one-to-ten.

27. The combination of Claim 21 wherein the  
5 beta-adrenergic antagonist comprises carvedilol or a pharmaceutically-acceptable salt thereof.

28. The combination of Claim 21 wherein the  
10 beta-adrenergic antagonist comprises metoprolol or a pharmaceutically-acceptable salt thereof.

29. The combination of Claim 21 wherein the  
15 beta-adrenergic antagonist comprises bisoprolol or a pharmaceutically-acceptable salt thereof.

30. The combination of Claim 21 wherein the  
20 beta-adrenergic antagonist comprises bucindolol or a pharmaceutically-acceptable salt thereof.

31. The combination of Claim 21 wherein the  
25 beta-adrenergic antagonist comprises propranolol or a pharmaceutically-acceptable salt thereof.

32. The combination of Claim 21 wherein the  
30 beta-adrenergic antagonist comprises esmolol or a pharmaceutically-acceptable salt thereof.

33. The combination of Claim 21 wherein the  
35 beta-adrenergic antagonist comprises acebutolol or a pharmaceutically-acceptable salt thereof.

34. The combination of Claim 21 wherein the  
40 beta-adrenergic antagonist comprises sotalol or a pharmaceutically-acceptable salt thereof.

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35. The combination of Claim 21 wherein the beta-adrenergic antagonist comprises labetalol or a pharmaceutically-acceptable salt thereof.

5 36. The combination of Claim 1 wherein said beta-adrenergic antagonist is selected from the group consisting of acebutolol, alprenolol, amosulalol, arotinolol, atenolol, befunolol, bevantolol, bisoprolol, bopindolol, bucumolol, bucindolol, bunitrolol,  
10 butofilolol, carteolol, carvedilol, celiprolol, cloranolol, indenolol, labetalol, levoprolol, mepindolol, metipranolol, metoprolol, nadolol, nebivolol, nifenalol, oxprenolol, penbutolol, pindolol, propranolol, sotalol, timolol, toprol, and viskenit.

15 37. The combination of Claim 1 wherein said beta-adrenergic antagonist is selected from the group consisting of Acc 9369, AMO-140, betaxolol, capsinolol, carazolol, CP-331684, diprafenone, ersentilide, esmolol,  
20 esprolol, Fr-172516, ISV-208, L-653328, laniolol, levobunolol, LM-2616, nipradilol, Pharmaprojects No 5279, S-atenolol, SB-226552, SR-58894A, SR-59230A, talinolol, tertatolol, tilisolol, TZC-5665, UK-1745, xamoterol, and YM-430.

25 38. The combination of Claim 36 wherein said aldosterone receptor antagonist is eplerenone.

30 39. The combination of Claim 37 wherein said aldosterone receptor antagonist is eplerenone.

40. The combination of Claim 36 wherein said aldosterone receptor antagonist is spironolactone.

35 41. The combination of Claim 37 wherein said aldosterone receptor antagonist is spironolactone.

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42. A pharmaceutical composition comprising a first amount of an aldosterone receptor antagonist and a second amount of a beta-adrenergic antagonist, wherein  
5 said aldosterone receptor antagonist and beta-adrenergic antagonist together comprise a therapeutically-effective amount of said aldosterone receptor antagonist and said beta-adrenergic antagonist.

10 43. The pharmaceutical composition of Claim 42 wherein said aldosterone receptor antagonist is selected from epoxy-containing compounds.

15 44. The pharmaceutical composition of Claim 43 wherein said epoxy-containing compound has an epoxy moiety fused to the "C" ring of the steroidal nucleus of a 20-spiroxane compound.

20 45. The pharmaceutical composition of Claim 44 wherein said 20-spiroxane compound is characterized by the presence of a 9a-,11a-substituted epoxy moiety.

25 46. The pharmaceutical composition of Claim 45 wherein said epoxy-steroidal-type compound is eplerenone.

47. The pharmaceutical composition of Claim 42 wherein said aldosterone receptor antagonist is  
30 spironolactone.

48. A therapeutic method for treating a cardiovascular disorder, said method comprising administering to a subject susceptible to or afflicted  
35 with such disorder a first amount of an aldosterone receptor antagonist and a second amount of a beta-adrenergic antagonist, wherein said aldosterone receptor

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antagonist and beta-adrenergic antagonist together comprise a therapeutically-effective amount of said aldosterone receptor antagonist and said beta-adrenergic antagonist.

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49. The method of Claim 48, wherein said cardiovascular disorder is selected from the group consisting of hypertension, congestive heart failure, cirrhosis and ascites.

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50. The method of Claim 49, wherein said cardiovascular disorder is hypertension.

51. The method of Claim 49, wherein said  
15 cardiovascular disorder is congestive heart failure.

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